

SEARCHING FOR BINDING SITES OF TOLL-LIKE RECEPTOR 4 (TLR4)

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Toll-like receptor 4(TLR4) responds to bacteria, virus and fungi. Inhibiting TLR4 can lead to the development of drugs that can be used for treating autoimmune disorders. A previous docking experiment has proposed a binding site for a TLR4 inhibitor known as Chitohexaose (Chrx). The present docking experiments include docking to be able to predict binding sites of TLR4 binding molecules including Chitohexaose (Chrx) and some other binders. The purpose for this is to be able to determine what specific characteristics of the binding site and develop a model for generating more potent TLR4 inhibitors with the ultimate goal of developing novel drugs to treat autoimmune disorders. We used the crystal structure of TLR4 for docking (PDB code 2Z64). TLR4 was prepared as receptor with and without its glycosidic modifications. Docking was conducted using Autodock vina. Three search space were created to cover the whole protein. Results from docking Chitohexaose (Chrx) showed the highest binding energy was -7.3 kcal/mol. There were two common binding sites. Docking other ligands (series 1) also resulted in observation of two common binding sites at which the highest binding energy was -8.4 kcal/mol. The binding sites for Chrx and series 1 were different and the difference can be a result of either a functional group added to series 1 and/or presence of the acetyl moieties on the molecules. Another finding was the bigger the size of the molecule the higher its affinity level. The amino acids that were common at both sites were histidine and glutamine.

Keywords: Chitohexaose, Toll-like receptors 4, Inhibitor